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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/403,269	10/18/1999	ULF LINDAHL	003300-589	7046

7590 02/26/2002

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EXAMINER
STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
1652	15

DATE MAILED: 02/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/403,269	ULF ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8 and 19-102* is/are pending in the application.

4a) Of the above claim(s) *8,19 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-24 and 26-102* is/are rejected.

7)☒ Claim(s) *25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application Status

Claims 8 and 19-102 are pending in the application.

Cancellation of claims 1, 2, 4-7, and 9-18 and addition of claims 21-102 in Paper No. 12 is acknowledged. Claim 3 was previously cancelled in Paper No. 9.

Claims 8, 19, and 20 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 9.

Applicants' request in Paper No. 12 for clarification of receipt of priority documents is acknowledged. All priority documents have been received.

Applicants' arguments filed in Paper No. 12 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

1. Claims 37, 59, 80, and 94 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 37, 59, 80, and 94 are confusing as a polynucleotide cannot be both a polynucleotide of a specific structure and an N-terminal, C-terminal, or an internal deletion variant of said structure simultaneously, but this is what is claimed. It is suggested that applicants clarify the meaning of the claim.

2. The written description rejection of claims 21-24 and 26-102 under 35 U.S.C. 112, first paragraph, is maintained. The rejection was fully explained in a previous Office action (Paper No. 10).

The claims are rejected because the specification does not contain any disclosure of the function of all polynucleotide sequences *comprising* a polynucleotide encoding the polypeptides of SEQ ID NOs:2-8 or amino acids 1-45, 25-45, 74-86, or 77-97 of SEQ ID NO:13, polynucleotides that hybridize thereto, polynucleotides that hybridize to SEQ ID NOs:9-11 or nucleotides 73-207, 73-1404, 73-3085, 145-207, 292-329, 301-362, 145-1404, 145-3085, 1-1404, and 1-3085 of the polynucleotide of SEQ ID NO:12, or deletion fragments thereof as encompassed by the claims. The genus of polynucleotides comprising the above described nucleic acid molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated polynucleotides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus of polynucleotides, i.e., the polynucleotide of SEQ ID NO:12, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicants argue that the specification provides sufficient written description and provide supporting details in the specification describing the characteristics and properties of the claimed genus of polynucleotides encoding C5-Epimerase polypeptides. It should be noted however, that applicants' claims are not in fact limited to polynucleotides encoding C5-epimerase polypeptides. Applicants' argument is not found persuasive. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case the claimed genera of polynucleotides includes species with the potentiality of being widely variant in function. The genus of claimed polynucleotides is functionally diverse as it encompasses polynucleotides encoding polypeptides with C5-Epimerase activity, those which lack such activity but are capable of inducing an antibody specific for the C5-Epimerase of SEQ ID NO:13, as well as an enormous number of polynucleotides encoding polypeptides with neither of these functions, but possibly other undisclosed functions, and further encompasses a significant number of oligonucleotides with a variety of functions. As such, neither the description of the structure and function of the polypeptide of SEQ ID NO:13 and the polynucleotide of SEQ ID NO:12 nor the disclosure of solely structural features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus.

3. The enablement rejection of claims claims 21 (a)-(d) and (g)-(m), 22-24, and 26-102 under 35 U.S.C. 112, first paragraph, is maintained. As stated in Paper No. 10, the specification, while being enabling for polynucleotides comprising nucleotides 73-1404 or 1-1404 of SEQ ID NO:12, does not reasonably provide enablement for polynucleotide sequences comprising a polynucleotide encoding the polypeptides of SEQ ID NOs:2-8 or amino acids 1-45, 25-45, 74-86, or 77-97 of SEQ ID NO:13, polynucleotides that hybridize thereto, polynucleotides that hybridize to SEQ ID NOs:9-11 or nucleotides 73-207, 73-1404, 73-3085, 145-207, 292-329, 301-362, 145-1404, 145-3085, 1-1404, and 1-3085 of the polynucleotide of SEQ ID NO:12, or deletion fragments thereof as encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants argue the specification provides sufficient enablement for isolation of the claimed genus of polynucleotides encoding a C5-Epimerase and provide supporting details in the specification

describing the characteristics and properties, e.g., substrates and enzymatic activity, of the claimed genus of polynucleotides encoding C5-Epimerase polypeptides. It should be noted however, that applicants' claims are not in fact limited to polynucleotides encoding C5-epimerase polypeptides. Applicants argue that the examiner has provided no support for the assertion of undue experimentation and no reason why a skilled artisan could not practice the claimed invention. Applicants' argument is not found persuasive. The examiner has provided support for undue experimentation and reasons why a skilled artisan could not make and/or use the claimed genus of polynucleotides by stating in a previous Office action (Paper No. 10), "[t]he specification does not support the broad scope of the claims... ...because the specification does not establish: (A) regions of the protein structure which may be modified without affecting glucuronyl C-5 epimerase activity; (B) the general tolerance of glucuronyl C-5 epimerase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any glucuronyl C-5 epimerase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful." Furthermore, the functional activity of a polypeptide is dependent on its structure, therefore, a polynucleotide comprising fragments of SEQ ID NO:12, fragments of polynucleotides encoding the polypeptide of SEQ ID NO:13, or polynucleotides hybridizing thereto as encompassed by the claims will not necessarily retain activity if found within a larger polypeptide and the contexts in which such activity will be maintained are highly unpredictable and the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Also, while methods to isolate functional homologues of a known sequence are well known to the skilled artisan, producing functional homologues or fragments as claimed by Applicants requires one of skill in the art to know or to be provided with guidance for the selection of which of the infinite number of homologues or fragments retain C5-Epimerase activity. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the claimed polynucleotides comprising fragments of SEQ ID NO:12, fragments of polynucleotides encoding the polypeptide of SEQ ID NO:13, or polynucleotides hybridizing thereto as encompassed by the claims for

C5-Epimerase activity. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification and therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 21, 31, 33, 38-40, 43, 53, 55, and 60-62 are rejected under 35 U.S.C. 102(b) as being anticipated by Wilson (Nature 368:32-38, 1994). Claims 21 and 31 are drawn to polynucleotides encoding a peptide selected from SEQ ID NOs:2-8 and fragments of SEQ ID NO:13 as encompassed by the claims. Claims 33, 38-40, 43, 53, 55, and 60-62 further limit the polynucleotides to DNA, vector sequences, and a host cell comprising said polynucleotides. Wilson teaches a DNA sequence encoding a polypeptide that is 100 % identical to the peptide of SEQ ID NO:7 (see attached sequence comparison). The DNA of Wilson was present as part of a cosmid clone (page 32). This anticipates claims 21, 31, 33, 38-40, 43, 53, 55, and 60-62 as written.

5. Claims 37, 59, 80, and 94 are rejected under 35 U.S.C. 102(b) as being anticipated by Voet (Biochemistry, 2nd Ed., John Wiley and Sons, Inc., 1995, page 966). Claims 37, 59, 80, and 94 are drawn to polynucleotides of claims 25-34, 47-56, 66-77, and 87-91 encoding a polypeptide with an N-terminal, C-terminal, or internal deletion. Voet teaches polynucleotides encoding single amino acids. This anticipates claims 37, 59, 80, and 94 as written.

6. Claims 86, 87, 90, 91, and 95-98 are rejected under 35 U.S.C. 102(b) as being anticipated by Xue (Cell 72:681-93, 1993). Claim 86 is drawn to polynucleotides or complements thereof that hybridize to an oligonucleotide selected from SEQ ID NOs:9-11 and claim 87 is drawn to the polynucleotide or complement thereof that hybridizes to the oligonucleotide selected of SEQ ID NO:9. Claims 90, 91, and 95-97 further limit the polynucleotides to DNA, RNA, vector sequences, and a host cell or E. coli host comprising said polynucleotides. Xue teaches a polynucleotide sequence that is 70 % identical to the peptide of SEQ ID NO:7 (see attached sequence comparison) and would hybridize to SEQ ID NO:7 under the specified conditions of claim 86. The polynucleotide of Xue was isolated as both DNA and RNA in a vector recovered from an E. coli host (page 691). This anticipates claims 86, 87, 90, 91, and 95-98 as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claim 99 is rejected under 35 U.S.C. 103(a) as being unpatentable over Xue. Claim 99 is drawn to a method for producing using a host of claim 97.

Xue disclose the teachings as described above. Xue do not teach a method of producing a polypeptide using their E. coli host cell.

Therefore, it would have been obvious to one of ordinary skill in the art to express a protein using a host cell comprising the DNA of Xue. One would have been motivated to produce a protein using a host cell comprising the DNA of Xue in order to characterize the encoded protein. One would have a reasonable expectation of success for producing a protein using a host cell comprising the DNA of Xue because of the results of Xue. Therefore, claim 99, drawn to a a method for producing using a host of claim 97 would have been obvious to one of ordinary skill in the art.

Conclusion

8. Claim 25 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

9. No claim is in condition for allowance. All claims are rejected.

Addition of claims 37, 59, 80, and 94 necessitated the new ground(s) of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The examiner can normally be reached Monday-Friday from 8:00 am to 4:30 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

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